Cell Biology

EFFECT OF *IN VIVO* ADMINISTRATION OF ANTI-CTLA-4 mAB AND IL-12 ON THE HUMORAL IMMUNE RESPONSE OF ORALLY TOLERIZED MICE

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Oral tolerance has been characterized as an immunological unresponsiveness to fed antigen. Normal (i.e., stimulatory) immune responses are induced when $CD4^+$ T cells receive two signals, one of which involves the interaction of B7 on APC's with CD28 on T cells. $CD4^+$ T cells receiving these signals are activated to proliferate and differentiate into cytokine-secreting Th1 or Th2 cells. Furthermore, cytokines are believed to play a primary role in $CD4^+$ T cell differentiation. IL-12 is thought to aid in Th1 development, typified by IFN-γ and IgG2a isotype production, while IL-4 leads primarily to a Th2 response, with IL-4 and IgG1 antibody production. Results from previous studies have indicated that the mechanism underlying the phenomenon of oral tolerance may involve the preferential interaction of B7 with CTLA-4 on the T cell rather than CD28. In this study, experiments were designed to determine if co-administration of IL-12 and anti-CTLA-4 mAb to mice (experimental mice) at the time of low-dose antigen feeding could abrogate suppression of humoral immune responses; control mice received rat IgG. Results showed that while orally tolerized control mice exhibited suppressed serum IgG2a levels, this suppression was not observed in mice treated with anti-CTLA-4 mAb and IL-12 at the time of feeding. In contrast, IgG1 and total (IgGMA) antibody levels remained suppressed in both experimental and control mice. These results suggests that anti-CTLA-4 mAb and IL-12 administration during low dose oral tolerance induction allows for differentiation of Th1 cells, which support the preferential differentiation of B cells into IgG2a-secreting plasma cells.